a reporter gene operatively linked to said transcription control element, wherein expression of said reporter gene mediated by said transcription control element causes expression of a reporter gene product that provides a detectable signal, wherein said detectable signal is detected optically by means selected from the group consisting of bioluminescence detection and fluorescence detection.

24. The biodetector of Claim 1, wherein said detectable signal is detectable by bioluminescence detection.

REMARKS

Introductory Comments

Claims 1-24 are pending. Claims 19-24 have been withdrawn from consideration. Claims 1-18 have been examined and rejected by the Examiner.

The Examiner has rejected claims 1-18 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over Contag, et al., (U.S. Patent No. 5,650,135, hereinafter referred to as '135) and Georgiou, et al., in view of Kasahara, et al.

These rejections are believed to be overcome in part by the amendments and are otherwise traversed for reasons discussed below.

Applicants acknowledge with appreciation the withdrawal of the previous rejection under 35 U.S.C. §112, second paragraph, and the withdrawal of the objection to claim 1.

Overview of the Amendments

Claim 1 has been amended to delete the numbering of the steps, and to state that the detectable signal is detected optically by means selected from the group consisting of bioluminescence detection and fluorescence detection. The amendment finds support in the claims as originally filed.

Claims 2 and 3 have been canceled without prejudice or disclaimer.

Claim 4 has been amended to depend from of claim 1 instead of the now canceled claim 3. The amendment corrects for dependency.

No new matter has been added by way of these amendments.

Rejection of Claims 1-18 Under 35 U.S.C. §103(a)

The Examiner has maintained the rejection of claims 1-18 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over Contag, et al., ('135) and Georgiou, et al., in view of Kasahara, et al. The Examiner agrees that the references do not provide a suggestion to combine or modify the references. However, the Examiner argues that the knowledge was generally available to one of ordinary skill in the art, and it would have been obvious to use the pho-P-phoQ operon disclosed by Kasahara *et al.* and the heterologous scFv disclosed by Georgiou *et al.* in order to take advantage of the increase in specificity, diversity and ease of production, and cites *In re Fine* and *In re Jones* in support. In addition, the Examiner states that hindsight reconstruction is permissible as long as it takes into account only the level of ordinary skill in the art, and does not include knowledge from the applicant's disclosure.

The applicants traverse the rejection. First, addressing the Examiner's arguments, in *In re Fine*, the claims were directed to a system for detecting and measuring minute quantities on nitrogen compounds comprising a gas chromatograph, a converter which converts nitrogen compounds into nitric oxide by combustion, and a nitric oxide detector. The primary reference disclosed a system for monitoring sulfur compounds comprising a chromatograph, combustion means, and a detector, and the secondary reference taught nitric oxide detectors. The Examiner and Board asserted that it would have been within the skill of the art to substitute one type of detector for another in the system of the primary reference, however the court reversed the rejection as it found there was no support or explanation of the position taken by the Office.

In *In re Jones*, the claimed invention was an amine-containing salt of dicamba, a compound with herbicidal activity. The primary reference disclosed substituted ammonium salts of dicamba as herbicides, however the reference did not specifically teach the claimed salt. Secondary references teaching the amine portion of the salt were directed to shampoo additives and a byproduct of the production of morpholine. Again,

the court found there was no suggestion to combine these references to arrive at the claimed invention.

The cited cases thus rejected the position taken by the Office that an invention is obvious if different references individually disclose all aspects of the invention. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination or without some objective reason to combine the teachings of the references. *In re Mills* 16 USPQ2d 1430 (Fed. Cir. 1990). The suggested desirability or an objective reason to combine the references is lacking in the present case.

In order to render claims obvious, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references. Second, there must be reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. The teachings or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Applicants submit that the cited references do not provide suggestion or motivation to combine the references, and they do not prove a reasonable expectation of success even if the references were combined. Thus, a *prima facie* case of obviousness has not been presented by the Office.

In the present case, there was no indication in the prior art that one of ordinary skill in the art would choose to create biodetectors wherein binding of target substance to the epitope-binding fragment of the ligand-specific binding domain activates the intracellular signal transforming domain, thus providing an activated intracellular signal transforming domain. The cited references merely disclosed different parts of the invention individually. Thus, the cited references do not provide a reason to pursue development of the biodetector constructs of the present invention, and do not provide any reasonable expectation of success even if the references were combined.

The Examiner states on page 5 of the Office Action that "it would have been obvious to said artisan to use the phoP-phoQ operon disclosed by Kasahara et al. and the

heterologous scFv disclosed by Georgiou et al. **in order to take the advantage of the increase in specificity, diversity, and ease of production of the resulting biodetector.**" (Emphasis original) The Examiner than states on page 7 that "the level of ordinary skill at the time the invention was made, it would have been obvious to the skilled artisan to use the phoP-phoQ operon disclosed by Kasahara et al. and the heterologous scFv disclosed by Georgiou et al. in the construct of Contag et al. in order to take advantage of the increase in specificity, diversity, and ease of production of the resulting biodetector. Additionally, by varying the scFv, one could easily create a library of biodetectors as taught by Georgiou et al." The motivation to combine or modify the references must be found in the references themselves or in the knowledge generally available to one of ordinary skill in the art. The cited references do not provide the motivation to combine the references as suggested by the Examiner. However, if the Examiner wishes to continue to cite the references to support his assertion, the applicants respectfully request that the Examiner provide a supporting affidavit.

In view of the above arguments, the applicants submit that the pending claims define an invention patentable over the cited prior art and that the rejections under 35 U.S.C. §103 should be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Please direct all further communications in this application to:

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If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned at (650) 325-7812.

Respectfully submitted,

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APPENDIX A

Marked up Version of The Claims.

1. (Twice amended) A biodetector for the detection of a selected substance, said biodetector comprising:

[(a)]a signal converting element, comprising (i) an extracellular ligand-specific binding domain which specifically binds said selected substance, wherein said ligand-specific binding domain comprises an epitope-binding fragment of an antibody, and (ii) an intracellular signal transforming domain, wherein binding of said substance to said epitope-binding fragment of said ligand-specific binding domain activates said intracellular signal transforming domain providing an activated intracellular signal transforming domain;

[(b)]a transducer, wherein (i) said transducer has an inactive form and an active form which are distinct from each other, and (ii) said activated intracellular signal transforming domain converts said inactive form of said transducer into said active form of said transducer;

[(c)]a transcription control element, wherein expression mediated by said transcription control element is activated by said active form of said transducer; and

[(d)]a reporter gene operatively linked to said transcription control element, wherein expression of said reporter gene mediated by said transcription control element causes expression of a reporter gene product that provides a detectable signal, wherein said detectable signal is detected optically by means selected from the group consisting of bioluminescence detection and fluorescence detection.

[2. (Cancel) The biodetector of Claim 1, wherein said detectable signal is detected optically.]

[3. (Cancel(The biodetector of Claim 2, wherein said detectable signal is detectable by means selected from the group consisting of bioluminescence detection, calorimetric reactions and fluorescence detection.]

4. (Twice Amended) The biodetector of Claim [3] 1, wherein said detectable signal is detectable by bioluminescence detection.